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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/706,801	11/12/2003	Francine M. Foss	00398-152001 / NEMC 263;	6989

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EXAMINER	
HAMUD, FOZIA M	

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 01/10/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/706,801	FOSS ET AL.	
	Examiner	Art Unit	
	Fozia M. Hamud	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 October 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-33* is/are pending in the application.

4a) Of the above claim(s) *12-30* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11, 31-33* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *08/12/2004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Detailed Office Action

1a. Applicant's election without traverse of the invention of Group I (claims 1-11 and 31-33) in the reply filed on 27 October 2005 is acknowledged.

Claims 1-33 are pending, of which claims 1-11 and 31-33 are under consideration by the Examiner. Claims 12-30 are withdrawn from further consideration by the Examiner, 37 C.F.R. § 1.142(b), as being drawn to a non-elected invention.

Information Disclosure Statement

2. The information disclosure statement (IDS) submitted 12 August 2002 has been received and complies with the provisions of 37 CFR §§1.97 and 1.98. It has been placed in the application file and the information referred to therein has been considered as to the merits.

Claim Rejections - 35 U.S.C. § 112:

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 1-7, 11 and 31-33 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated polypeptide comprising the polypeptide of SEQ ID NO:1, wherein there is a mutation at the position corresponding to position 143 of said SEQ ID NO:1, does not reasonably provide enablement for a substantially pure polypeptide comprising an amino acid sequence that is identical to wild type IL-7 sequence, where there is one or more amino acid residues in t he carboxy-terminal helix D region is mutant, or where there is an addition,

deletion or substitution at positions 136-144 of SEQ ID NO:1. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, how to make or use the invention commensurate in scope with these claims.

Claims 1-7, 11, 3-33 are drawn to an IL-7 mutant wherein there is one or more mutant amino acid residues in the carboxy-helix D region, or where there is an addition, deletion or substitution at positions 136-144 of SEQ ID NO:1. However, the instant specification discloses only IL-7 mutants where there is substitutions at position 143, for example, where tryptophan at position 143 is substituted with alanine, histidine, tyrosine, praline, (see page 20, lines 21-28). The specification further discloses that said mutants bind to IL-7 receptor with less affinity compared to native IL-7 and induce proliferation of IL-7 dependent 2E8 cells, (see page 18, lines 26-30). The instant specification does not disclose any other mutant where position other than amino acid residue 143 has been substituted, from any other species. Neither does the specification disclose an IL-7 mutant where there is an addition, deletion at positions 136-144 of SEQ ID NO:1. Furthermore, it is known for proteins that even a single amino acid change or mutation can destroy the function of protein in many instances, albeit not in all cases. The effects of these changes are largely unpredictable as to which ones have a significant effect versus not. Several publications document this unpredictability of the relationship between sequence and function, albeit that certain specific sequences may be found to be conserved over proteins of related function upon a significant amount of further research (see Wells, 1990, Biochemistry 29:8509-8517).

To practice the instant invention in a manner consistent with the breadth of the claims would not require just a repetition of the work that is described in the instant application but a substantial inventive contribution on the part of a practitioner which would involve the determination of which carboxy terminal amino acid residues of the IL-7 of SEQ ID NO:1, besides amino acid residue 143 of SEQ ID NO:1, would tolerate deletion or substitution and would still retain the desired activity. It is this additional characterization of the disclosed protein that is required in order to obtain the functional and structural data needed to permit one to produce a polypeptide which meets both the structural and functional requirements of the instant claim that constitutes undue experimentation. The criteria set forth in Ex parte Forman (230 USPQ 546 (Bd. Pat. App. & Int. 1986), and reiterated in In re Wands (858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)), which include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art and (8) the breadth of the claims, is the basis for determining undue extermination. In the instant case, Due to the large quantity of experimentation necessary to generate the infinite number of IL-7 mutants recited in the claims and possibly screen same for activity, the lack of direction/guidance presented in the specification regarding which residues tolerate alterations, where to add additional amino acid residues, in order to provide activity, the absence of working examples directed to same, the complex nature of the invention, the state of the prior art which establishes the unpredictability of the effects of

mutation on structure and function, and the breadth of the claims which fail to recite any structural or functional limitations, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

Claim Rejections - 35 U.S.C. § 112:

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 1-11 and 31-33 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

4a. The term "substantially pure" recited in claim 1 is a relative term which renders the claim indefinite. The term "substantially pure" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, i.e, how pure should the claimed polypeptide be, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. Appropriate correction is required.

4b. Claims 1, 3, 4, 5 recite "one or more amino acid ...", however, it is unclear how many amino acid residues should be altered, if more than one. The metes and bounds of the claim can not be ascertained.

Claims 2, 6-11 and 31-33 are vague and indefinite so far as they depend from claim 1 for the limitations set forth directly above.

Priority

5. Applicant's claim for priority under 35 U.S.C. 119(e) U.S. Provisional Application No: 60/425,925 (12 November 2002) is acknowledged. Thus the effective fling date of 12 November 2002 is used for the purposes of applying prior art.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

6a. Claims 1-2, 8-11and 31 are rejected under 35 U.S.C. 102(a) VanderSpeck et al (March 2002).

VanderSpeck et al disclose several IL-7 mutants where in tryptophan residue of wild type human IL-7 has been replaced with either alanine, histidine, tyrosine or proline, (page 227). The authors studied binding affinity of the IL-7 mutants and its ability to stimulate DNA synthesis of 2E8 cells. They demonstrated that the substitution at position 143 of IL-7, resulted in mutants that bind binding to IL-7R and subsequently stimulate of DNA synthesis of 2E8 cells, albeit to differing degrees, (see figures 2 and 4).

The instant claims 1, 2, 8-11 and 31 are drawn to IL-7 mutant polypeptides, wherein there is an alteration at the carboxy terminal, at positions 136-144 and specifically at position 143 and where in said mutant effectively competes with wild type IL-7 for binding.

Therefore, the VanderSpeck et al reference meets all the limitations recited in instant claims 1, 2, 8-11 and 31, thus anticipating theses claims in the absence of any evidence on the contrary.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6b. Claim 1 is rejected under 35 U.S.C. 102(b) Gregoire et al (October 2001).

Gregoire et al disclose an IL-7 mutant that comprises several amino acid residues that are different than those found in the polypeptide of SEQ ID NO:1, at the carboxy terminal. See attached copies of the comparison of instant SEQ ID No: 1 and the sequences of the reference (SEQUENCE COMPARISON A).

The instant claim 1 is drawn to an IL-7 mutant polypeptide, wherein there is an alteration at the carboxy terminal. Therefore, the Gregoire et al reference meets all the limitations recited in instant claims 1, thus anticipating instant claim 1 in the absence of any evidence on the contrary.

Claim Rejections under 35 U.S.C. §103:

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7a. Claims 1 and 32-33 are rejected under 35 U.S.C. 103(a) as being unpatentable over VanderSpeck et al in view of Capon et al., U.S. Patent Number 5,116,964.

The teachings of VanderSpeck et al in are discussed above. However, VanderSpeck et al does not teach a chimeric polypeptide comprising the polypeptide of VanderSpeck et al fused to a heterologous polypeptide.

Capon teaches fusion proteins comprising immunoglobulin polypeptide fused to "ligand binding partners", which are defined as including hormones and growth factors (see column 2, lines 14-19). At column 4, lines 38-43, Capon states that the immunoglobulin (Ig) fusions of the invention "serve to prolong the in vivo plasma half-life of the ligand binding partner..." and "facilitate its purification by protein A". Also taught are recombinant materials for making such a fusion protein, vectors and expression; see columns 15-16. Preferred embodiments include sequences including the hinge regions of IgG-1, -2, -3 or -4, IgA, IgE, IgD and IgM, see column 14, lines 40-45 (the first domain of the constant region can be omitted). The preferred species of Ig was human, see claims 8-9. Capon states that the DNA sequences for the Ig chains were well known in the art at the time the invention was made, see column 15 beginning at line 40.

Therefore, it would have been obvious to the person of ordinary skill in the art at the time the invention was made to modify the polypeptide of VanderSpeck et al to make fusion proteins as taught by Capon et al. The person of ordinary skill in the art would have been motivated to make the modification in view of Capon's disclosure that fusion proteins facilitate purification of desired proteins and prolong the in vivo half life.

Accordingly, the invention, taken as a whole, is prima facie obvious over the cited prior art.

Conclusion

7. No claims are allowed.

Advisory Information:

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Fozia M. Hamud whose telephone number is (571) 272-0884. The examiner can normally be reached on Monday, Thursday-Friday, 6:00 am to 4:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda G. Brumback can be reached on (571) 272-0961. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Fozia Hamud
Patent Examiner
Art Unit 1647
06 January 2006

Eileen B. O'Hara

EILEEN B. O'HARA
PATENT EXAMINER